

Amendments to the specification

Please amend the paragraph beginning at page 33, line 24, as follows:

B1
In a preferred embodiment the protein is a human protein. In more preferred embodiments, the protein is human Factor VIII and the protein is a B domain deleted human Factor VIII. In another preferred embodiment the protein is B domain deleted human Factor VIII with a sequence which includes a recognition site for an intracellular protease of the PACE/furin class, such as ~~X-ARG X-X-ARG~~ X-Arg-X-X-Arg site, a short-peptide linker, e.g., a two peptide linker, e.g., a leucine-glutamic acid peptide linker (LE), or a three, or four peptide linker, inserted at the heavy-light chain junction (see Fig. 1).

Amend the paragraph beginning at page 68, line 15, as follows:

B2
The construct for the expression of human Factor IX (Figure 16), pXIX76, is a 8.4 kilobase (kb) circular DNA plasmid which contains the following elements: a cytomegalovirus (CMV) immediate early I gene 5' flanking region comprising a promoter sequence, 5' untranslated sequence (5'UTS) and a first intron sequence (~~equivalent to nucleotides 174328–172767 of Genbank Accession X17403~~). The CMV region is next fused with a wild-type Factor IX cDNA sequence, with a BamHI site at the junction. The Factor IX cDNA sequence is next fused to a 1.5 kb fragment from the 3' region of the Factor IX gene that includes the transcription termination signal (~~equivalent to nucleotides 34335–35857 of Genbank Accession K02402~~). A selectable marker gene (the bacterial neomycin phosphotransferase gene (neo)) to allow selection for stably transfected mammalian cells using the neomycin analog G418 is inserted upstream of the CMV sequences. Expression of the neo gene is under the control of the herpes simplex virus thymidine kinase promoter. ~~The neo expression cassette is equivalent to [nucleotides 452–1596 of Genbank Accession U43612~~. The pUC19 – based amplicon carrying the pBR322-derived beta-lactamase gene and origin of replication allows for the selection and propagation of the plasmid in *E. coli*.

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Amend the paragraph beginning at page 70, line 15, as follows:

B3
The construct for the expression of human α -galactosidase, plasmid pXAG94 (Figure 18) is a 8.5kb circular DNA plasmid which contains the following elements. A selectable marker gene (the bacterial neomycin phosphotransferase gene (neo)) is inserted upstream of the α -galactosidase expression cassette to allow selection for stably transfected mammalian cells using the neomycin analog G418. Expression of the neo gene is under the control of the SV40 early promoter. Specifically, the 342 bp ~~PvuII – HindIII~~ fragment equivalent to nucleotides 273 – 1/5243 – 5172 of Genbank Accession J02400 is fused via a Xhol linker to a fragment equivalent to nucleotides 502 – 561 of Genbank Accession J02400, which is next fused to the neo coding region, equivalent to nucleotides 350 – 1322 of Genbank Accession U13862. Polyadenylation signals for this expression cassette are supplied by sequences 3393 – 3634 of SYNPRSVNEO. This selectable marker is fused to a short plasmid sequence, equivalent to nucleotides 2067 (PvuII) – 2122 of SYNPBR322.

Amend the paragraph beginning at page 70, line 27, as follows:

B4
Expression of the α -galactosidase cDNA is directed from a CMV enhancer (~~equivalent to nucleotides 174253 – 173848 of Genbank Accession X17403~~). This DNA is fused via the linker sequence TCGACAAGCCGAATTCCAGCACACTGGCGGCCGTTACTAGTGGATCCGAG (SEQ ID NO:107) to human elongation factor 1 α sequences extending from –207 to +982 nucleotides relative to the cap site. These sequences provide the EF1 alpha promoter, CAP site and a 943 nucleotide intron present in the 5' untranslated sequences of this gene. The DNA is next fused to the linker sequence

GAATTCTCTAGATCGAATT CCTGCAGCCCCGGGGATCCACC (SEQ ID NO:108) followed immediately by 335 nucleotides of the human growth hormone gene, starting with the ATG initiator codon, ~~equivalent to nucleotides 5225 – 5559 of Genbank Accession J03071~~. This DNA codes for the signal peptide of the hGH gene, including the first intron.

Amend the paragraph beginning at page 71, line 9, as follows:

B5
This DNA is next fused to the portion of the wild-type α -galactosidase cDNA that codes for amino acids 31 to 429. The coding region is next fused via the linker

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AAAAAAAAAAACTCGAGCTCTAG (SEQ ID NO:109) to the 3' untranslated region of the hGH gene, corresponding to nucleotides 6699 – 7321 of Genbank Accession J03071. Finally, this DNA is fused to a pUC – based amplicon carrying the pBR322-derived beta-lactamase gene and origin of replication which allows for the selection and propagation of the plasmid in *E. coli*; the sequences are equivalent to nucleotides 229 – 1/2680 – 281 of SYN PUC12V.
